بسم الله الرحمن الرحيم

University of Khartoum

Graduate College

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CLINICAL AND ECHOCARDIOGRAPHIC FINDINGS IN CHILDREN WITH MALNUTRITION IN KHARTOUM STATE.

By

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M.B.B.S. (Omdurman Islamic University).

A thesis submitted in partial fulfillment for the requirements of the degree of Clinical MD in Paediatrics & Child Health, May 2007

Supervisor

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Prevalence of Schneider's first-rank symptoms

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May2007

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DEDICATION

TO

All My Family Members

My Parents

My Husband Dr: Almohaisi

My Kids

For Their Patience and Love

To

All My Teachers

And My Colleagues

For Their Continuous Advice and Support

To

All Malnourished Children

For Brighter Tomorrow

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Abstract

Protein Energy Malnutrition (PEM) is a common paediatric problem in Sudan.

The pathogenesis of severe malnutrition was suggested to affect the heart .The aims of this study were to determine the cardiac clinical manifestations, Echocardiographic abnormalities in severe malnourished children and to compare heart abnormalities in a group of malnourished children with control group and to describe their predictive values.

The study was prospective, hospital based, case-control study. Fifty seven severely malnourished children taken as study group and eighteen healthy age and sex matched children were taken as control group. All malnourished children were subjected to full history taking, through clinical and anthropometric measurements. Echocardiography and chest X-Ray were also performed. Laboratory investigations were performed including Hb%, PCV, serum albumin and electrolytes. While in control group echocardiography was done.

Fifty six percent of the study group were <18 months of age, and female were account about 61.4%. 55% of study group were from western tribes.63% of patients were from urban areas and 37% were from rural areas.

Clinical manifestations of cardiovascular system in the study group were sudden weight gain in 25%,dysponea in 12%and cyanosis in 1%.Tachycardia in 27%,large volume pulse in 13%and Bradycardia in 2% .Heart failure in 4%.75% of patients had low haemoglobin level, hypocalcaemia founds in 91%, Hyponatraemiaty in 49%, hypokalaemia in 45%. Regarding the result of the chest X-Ray, cardiomegally found in 5%, consolidation in 40%. Regarding Echocardiographic findings, the LVM was significant reduced in patients with PEM compared with control group (mean 11.38±7.74 vs 22.23±12.03), LVMI was (kg/m^2) was reduced in patients compared with controls (32.34±20.4 vs 47.58 ±23.45), however, it was markedly reduced in kwashiorkor (23.88 ±18.56 vs 47.58 ±23.45), no statistically significant in IVSs and IVSd in patients compared with controls.

PWTs was significant reduced in patients compared with control (0.56±0.13 vs 0.66±0.18). PWTd showed no significant different in all patients compared with controls. LVIDs was significant different in patients with kwashiorkor compared with controls (1.40±0.27vs1.66±0.29) but LVIDd showed no significant difference in all study group compared with controls. Regarding systolic function, EF and FS were reduced in patients compared with controls (mean 67.71 ±9.25 vs 74.69 ±6.73) and (36.35±7.39 vs 41.13±4.98).while in diastolic function, A wave and E/A ratio were showed no change in patients compared with controls but E wave was statistically significant in all three groups of malnutrition.

This study concluded that severe malnutrition regardless of its type has definitive affection in heart muscles. Systolic function was affected more than diastolic function. Particular care with fluid administration is mandatory specially during the early phases of management, when heart function is the most compromise.

ملخص الاطروحة

يعتبر مرض سوء التغذية من مشاكل الاطفال الشائعة في السودان وقد اقترحت الدراسات السابقة تأثير امراضية سوء التغذية الوخيم علي القلب .

تهدف هذه الدراسة لتحديد مدي اثر سوء التغذية الوخيم علي القلب وذلك بمعرفة التظاهرات السريرية القلبية وتحديد الشذوذات الموجودة في تخطيط القلب بالصدي للاطفال المصابين بسوء التغذية مقارنة بنتائج دراسة تخطيط القلب بالصدي للمجموعة الضابطة ووصف القيم التنبؤية .

أجريت هذه الدراسة بالمستشفي وهي دراسة استقرائيه وصفية علي اساس المنهج المستقبلي وضبط الحالة .

شملت الدراسة 57 طفلا من الاطفال المصابين بسوء التغذية المنومين بالمستشفي وثمانية عشر طفلا من الاطفال الاصحاء من نفس الجنس والعمر كمجموعة ضابطة .

وقد تم اخضاع كافة الاطفال المصابين للبحث بتدوين حالاتهم التاريخية الكاملة من خلال فحوصات سريرة واجراء قياسات النمو لهم – كما أجري لهم تخطيط القلب بالصدي واخذ صورة اشعة للصدر .

اضافة لذلك تم عمل فحوصات معملية شملت فحص نسبة الخضاب بالدم وحجم الخلايا الحمراء وفحوصات الزلال المصلي والمنحلات الكهربائية (الالكترونيات) بينما تم فقط عمل تخطيط القلب بالصدي لمجموعة الضبط.

كانت نسبة 56% من الاطفال في مجموعة الدراسة أعمارهم أقل من 18 شهر وكانت نسبة الاناث تشكل 61.4% . ووجد ان نسبة 55% منهم كانت من قبائل غرب السودان و 63% من المرضي من المناطق الحضرية و 37% من المناطق الريفية .

أوضحت الاعراض السريرية للجهاز الوعائي القلبي في مجموعة الدراسة ان هناك نسبة 25% منهم اكتسبوا وزنا فجائيا وان 12% منهم يعانون من زلة تنفسية و 1% من الازرقاق و 27% من خفقان القلب و 13% من نبضات ذات حجم كبير و 2% بطء قلبي – وقد تم اكتشاف حالات فشل قلبي في 4% واتضح ان 75% من المرضي لديهم مستوي خضاب منخفض. كما وجد ان 91% يعانون من تدني في كلس الدم و 49% من تدني في صوديوم الدم و 45% من تدني في بوتاسيوم الدم .

اما فيما يختص بنتائج صور الاشعة السينية وجد ان نسبة 5% يعانون من حالة تضخم في القلب و 40% من تصلد الرئة .

وفيما يختص بموجودات او نتائج تخطيط القلب بالصدي وجد ان كتلة البطين الايسر تقلصت بشكل ملحوظ عندما المرضي المصابين بسوء التغذية عند مقارنتهم بمجموعة الضبط (متوسط 22.23 ± 12.03 مقابل 11.38 ± 7.74) . ولوحظ كذلك ان مؤشر كتلة البطين الايسر (كجم/م2) كان متدنيا في المرضي عند مقارنتهم بمجموعة الضبط ($47.58 \pm 23{,}45$ مقابل $32{,}34 \pm 20.4$) . وفي العموم قد وجد متدنيا بشكل ملحوظ عند الاطفال الذين يعانون من مرض سوء التغذية .

لم يلاحظ اي اختلافات احصائية معتبره للحاجز البطيني الداخلي سواء في حالة الانقباض او الانبساط عند المرضي عند مقارنتهم بمجموعة الضبط ووجد ان سمك الجدار الخلفي في حالة الانقباض كان متدنيا بدرجة ملحوظة عند المرضي عند مقارنتهم بمجموعة الضبط ($56, \pm 13,$

مقابل ‎66, ± 18,)‎ . لذلك اتضح بأنه لايوجد اختلافا معتبرا في سمك الجدار الخلفي في حالة انبساط القلب عند جميع المرضي عند مقارنتهم بمجموعة الضبط , ووجد ان الحد الداخلي للبطين الايسر في حالة انقباض القلب كان مختلفا بشكل واضح عند مرضي الكواشكور عند مقارنتهم بمجموعة الضبط بمتوسط ‎(1,66 ± 29,‎ مقابل ‎1,40 ± 27,)‎.

الا ان الحد الداخلي للبطين الايسر في حالة الانبساط لم يظهر اختلافا عند جميع مرضي مجموعة الدراسة عند مقارنتهم بمجموعة الضبط .

اما فيما يختص بالوظائف الانقباضية للقلب وجد ان جزئي الافراغ والتقصير كانا متدنيين في المرضي عند مقارنتهم مع مجموعة الضبط بمتوسط ‎(67,71 ± 9,25‎ مقابل ‎74,69 ± 6,73)‎ و ‎(36,35 ± 7,39‎ مقابل ‎41,13 ± 4,98)‎.

وكان واضحا ان الوظائف الانبساطية للقلب حسب ماوضحته الموجه (أ) ومعدل الموجة هـ/أ لم يطرأ عليها اي تغيير عند المرضي عندما تمت مقارنتهم مع مجموعة الضبط الا ان الموجه (هـ) اوضحت اختلافا احصائيا معتبرا في كافة المجموعات التي تعاني من سوء التغذية عند مقارنتهم بمجموعة الضبط .

اضافة الي ذلك من المتغيرات التي وجدت عند مرضي سوء التغذية الانصباب التاموري وحركة الحاجز البطيني التناقضية وانعكاس معدل الموجات هـ/أ وتراكم الموجات أ و هـ .

خلصت هذه الدراسة بأن مرضي سوء التغذية الوخيم بغض النظر عن نوعه لديه تأثيرا واضح علي عضلات القلب وان وظائف القلب الانقباضية اكثر تأثيرا من وظائفة الانبساطية , لذا يتوجب العناية الخاصة عند العلاج بالسوائل الوريدية خصوصا في المراحل المبكرة للعلاج اذ ان وظيفة القلب تكون حينها اكثر عرضه للخطر .

List of abbreviations

ASE	American Society to Echo – Cardiology .
A VTI	A velocity time integral .
CTR	Cardiothoracic Ratio.
CXR	Chest X Ray .
Dd	end Diastolic Dimension .
Ds	end Systolic Dimension .
ECG	Electrocardiogram .
EDT	Deceleration Time of peak E velocity.
E F	Ejection Fraction .
F S	Fraction Shortening .
E VTI	E velocity time integral.
F S	Fraction Shortening .
IVSd	Interventricular septal thickness in diastole.\
IVSs	Interventricular septal thickness in systole.
LEVDd	Left Ventricular End Diastolic Diameter .
LVIDd	Left Ventricular Internal Dimension in end diastole.
LVIDs	Left Ventricular Internal Dimension in end systole
LV	Left Ventricle**.**
LVM	Left ventricular mass .
LVMI	Left ventricular mass Index .
MUAC	Mid Upper Arm Circumference .
PEM	Protein Energy Malnutrition.
PWTd	Left Ventricular Posterior Wall Thickness in diastole.
PWTs	Left Ventricular Posterior Wall Thickness in systole.
QTc	Corrected QT interval .
QTd	QT interval dispersion.
SD	Stander Deviation.
SPSS	Statistical Package of Social Sciences
USA	United State of America.
WHO	World Health Organization .

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Chapter One

1- INTRODUCTION AND LITERATURE REVIEW

1.1 General Consideration:

The World Health Organization defines malnutrition as “The cellular imbalance” between supply of nutrients and energy and the body’s demand for them to ensure growth, maintenance and specific functions[(1)].

Also protein energy malnutrition (PEM) is defined as arrange of pathological conditions arising from coincident lack in varying proportions of protein and calories, occurring most frequently in infants and young children[(2,3)]. Malnutrition is globally the most important risk factor for illness and death, contributing to more than half of deaths in children worldwide(1). (PEM) first described in the 1920s, is observed most frequently in developing countries[(1)]. It’s directly responsible for

300,000 deaths per year in children younger than 5 years in developing countries and contributes indirectly to over half the deaths in childhood worldwide(1).

Risk Factors :

Health or diseases are the resultant of interaction between man and his environment. The tropical and subtropical areas of the world have at the present time, ecological conditions favoring the greater frequency and severity of certain pathological conditions among which are the nutritional deficiencies. This is not primarily related to the physical characteristics of the environment, but more to the biological and particularly to the socio-economic characteristics of these areas[(4-7)]. Malnutrition is a complex condition that can involve multiple, over-lapping deficiencies of protein, energy and micronutrients. A child becomes malnourished because of illness in combination with inadequate food intake. Insufficient access to food, poor health services, the lack of safe water and sanitation, and inadequate child and maternal care are underlying causes [8].

Children as organisms in the process of growth and development, being less prepared to confront the adverse forces of environment, are particularly prone to suffer the unfavorable ecological conditions more than the adult population. In the particular case of nutritional deficiency, they also have proportionately greater nutritional requirements than adults for the most essential nutrients. All these factors explain why nutritional deficiencies are, at the present time, one of the major health problems in the tropical and subtropical regions and why the problem is particularly serious in children [9-11].

A study done in south India, where more than 20% of children under four years suffer from acute malnutrition, suggested that the gender of the child and socioeconomic factors were stronger risk factors for malnutrition than health-care availability and health-care-seeking attitudes. The father's occupation was amore accurate indicator for malnutrition than household income.

In Sudan a study done by Dr. Hayat Osman (1983) found that late introduction of supplementary feeding, low socio-economic status, high illiteracy rate among mothers, position of the child within the family are closely related to etiology of malnutrition in the Sudan [13].

Also in Northern Sudan in 1988 Coulter JB and Suleiman G found that factors in the group with PEM which could relate to a etiology include, a history of prolonged illness and anorexia, frequent and prolonged episodes of diarrheoa and recent measles [14].

The immediate determinants of child nutritional status are in turn, influenced by three underlying factors manifesting themselves at the household level. These are, food security, adequate care for mothers and children and proper health environment. Including access to health services [15].

Overview of Malnutrition:

1- Global:

Protein energy malnutrition in its many forms, including under nutrition, specific nutritional deficiency and over nutrition, persists in virtually all countries world wide inspite of the general improvement in food supply and health conditions, and the availability of education and social services [16]. The rates of under nutrition and stunting have continued to rise in Africa from 24% to 26.8% and 47.3% to 48% respectively since 1990. With the worst increases occurring in the eastern region of Africa(1) .

The World Health Organization (WHO) global database on protein energy malnutrition and child growth; which covers 87% of the total population of infants and young children in developing countries, found that the prevalence of protein energy malnutrition in developing countries, worldwide, had progressively fallen from 42.6% in 1975 to 34.6% in 1995 . However, in some regions such as Africa and South East Asia, the actual number of malnourished children has risen. Over two thirds of the world's malnutrition cases live in Asia, whilst 17% are in Africa and 3% in Latin America.

The (WHO) estimates that by the year 2015, the prevalence of malnutrition will decrease to 17.6% globally, with 113.4 million children younger than 5 years being affected. The overwhelming majority of these children, 112.8 million will be living in developing countries, 70% in Asia, particularly the southern central region and 26% in Africa. In addition 165 million (29.0%) children will be stunted secondary to poor nutrition(1).

Currently more than half of young children in South East Asia have PEM, which is 6.5 times the prevalence in western hemisphere [1],In sub-Saharan Africa, 30% of children have PEM(1).

In Chad they found that the prevalence of severe malnutrition is 37% and mortality was significant higher in severely malnourished children with diarrhea, and respiratory infections [17].

In Zaire, it was found that severe malnutrition causes 16% of deaths in children under five years in the rural area of Bwamanda [18].

In USA, the incidence of malnutrition is less than 10% even in highest risk group studies of hospitalized children studies that as many as one fourth of patient had some form of acute PEM and 27% had chronic PEM [1].

Experience in Sudan:

Sudan's geography and ecology is an important structural factor shaping the health, nutrition and population situation. Poverty in Sudan is deep and widespread. Although data is not available for poverty measurement, child mortality and malnutrition are considered to reflect the underlying household economic conditions. Not only does Sudan experience high rates of mortality and malnutrition, but survey data show that these are quite evenly distributed over most of the socio-economic spectrum. Decades of civil war have had a severe impact on Sudan's economic and social development®.

Malnutrition is at chronically high level throughout Sudan, in both urban and rural areas, and is a major cause of death in humanitarian crisis situations. Chronic malnutrition among under 5 children in North Sudan is estimated at 36% while the prevalence of acute malnutrition in southern Sudan is as high as 15 to 20% [R].

In a survey in Al Haj Yousif area, Bushara found that the percentage of marasmus was 3.9% and kwashiorkor was 2.6% of the total children [20]. Zumrawi et al studied a group of infant longitudinally from birth to one year in urban poor neighborhoods in Khartoum province, 50% of children were found to be under nourished [21]. In Eastern Sudan, a study was done in 73 rural communities and more than 50% of children were found to be underweight [22].

A survey conducted by the Ministry of Health between 1986-87, found that 32.1% of children under 5-years were stunted, 14.1% were underweight and 1.7% were having severe malnutrition [23].

Other surveys of the Ministry of Health – Sudan showed that under nutrition was a prevalent problem among most of the provinces ranging from 10.2% in Khartoum to 26.6% in Sennar State [24].

In 1997 study done by Nestel PS found the prevalence of under nutrition among infants and young children was very high in Sudan. Moderate to severe forms of malnutrition ranged from 20-40% of under five years Sudanese children [25].

In 1997 a nutritional survey in Khartoum State, revealed that16.6% of 2775 children studied were malnourished 3.4% of them were severely malnourished [26].

Assessment of Malnourished Children:

Physical measurements like body weight and height of children have been extensively used to define health and nutritional status of children in the community[27-29].

Weight chart:

A child's weight is a good indicator of his nutritional status, especially if he is under 5 years of age. It requires a considerable skill to decide from a single or even a series of weight measurements whether or not a child is growing satisfactorily. However, this can be done quite easily if the weights are compared to normal or reference weights of children of the age or height. The best and simplest way to do this is to plot the weight of the child on a weight chart on which the reference weight are already drawn[27].

The upper line of the chart corresponds approximately to the average weight of healthy children and the lower line to approximately 80% of this. More precisely the upper line represents the 50th centile for boys and the lower, the third centile for girls of the WHO "reference weights". The space between the two lines has been called the "road to health" [27].

The weight curve should increase at about the same rate as the "reference" curves. If the child is not gaining weight or is losing weight, the curve will be flat or down - going, and such a child needs special care[44,49]. There is no doubt that if the road to health chart is used regularly and with care, malnutrition can be detected at an early stage and treatment started before it is too late.

Weight for age:

It is the single measure most commonly used in growth monitoring programmes world wide [31,32]. The weight of the child is expressed as a percentage of the expected weight of a healthy child of the same age [2,33]. This was introduced by Gomez et al to classify protein-energy malnutrition [2,35-34]. Weight for age is a sensitive index of growth faltering, demarcating the road to health[36].

Height for age:

The height of a child is expressed as a percentage of the reference height for his age and it indicates whether or notes the child is stunted. However it is impossible to tell from his height whether the child is also malnourished(27).

Weight for height:

It is important to distinguish between thin children and stunted children. The best way to identify thin children is to measure both their weight and heights. Then it can be seen, using a table, whether or not the weight is in the normal range for a child of similar height [27,37].

Arm circumference:

Between one year and five years, the upper arm circumference of healthy children remains fairly constant at about 16 cm. If the child becomes malnourished. The circumference is reduced. Therefore measuring the mid upper arm circumference can be useful and quick screening method for finding malnourished children of 1-5 years of age [3,27].

The arm circumference is measured with a nonstretchable tape. If it is between 12.5 and 13.5 cm, the child can be considered as moderately malnourished. Values below 12.5 cm indicate sever malnutrition. Arm circumference is readily available form of technology requiring no scales, measuring devices or graph plotting, costs very little and is easy to learn(31, 38,39) .

It should be realized that arm circumference is not as accurate an indicator of protein energy malnutrition as the weight for age and weight for height, and it cannot be used to monitor the progress in the individual child. (30)

Classification of Childhood Malnutrition:

The widely used classifications of childhood malnutrition are:

(1) Gomez classification

(2) Welcome trust classification

(3) Water low classification

(4) WHO classification

(5) Mid upper arm circumference (MUAC) classification.

Gomez classification:

The only method of classification in wide spread day to day use is the Gomez classification, in which the weight for age of a patient is calculated according to a standard as follows [2,40-42].

1- Normal patients having more than 90% of the expected weight to age.

2- Mild (first degree malnutrition, having 89-75% of the expected weight for age.

3- Moderate (second degree malnutrition) having 74-60% of the expected weight for age.

4- Severe (third degree) in which patients either have less than 60% of the expected weight for age or have lower limbs oedema.

Welcome trust classification:

It uses weight for age and present of nutritional oedema to classify the nutritional status of children [2,38-40].

1- Weight for age less than 60% without oedema is marasmus, with oedema is marasmic kwashiorkor.

2- Weight for age 61-80% without oedema is under weight, with oedema is kwashiorkor

3- Weight for age more than 80% with out oedema is well nourished child with oedema is kwashiorkor .

Water low classification:

It classifies stunting, which represent chronic malnutrition ,into three degrees using height for age :-

1-more than 95% is normal .

2-first degree 95%_90%.

3-second degree 89%_85% .

4-third degree less than 85% .

Also called the present malnutrition ,wasting, measured by loss of weight related to height .if the weight for height :-

1- More than 90% there is no wasting .

2- 90%_80% there is first degree wasting .

3- 80_70%there is second degree wasting .

4- Less than 70% there is third degree wasting .(1,48,51,52,53)

Use of mid upper arm circumference to classify malnutrition :-

Mid upper arm circumference had been proposed as an alternative index of use where the collection of height and weight measurement were difficult ,including emergency situation such as famines or refugee crises. In these situation ,low MUAC ,based on affixed cut-off point such as 12.5 cm had been used as a proxy for low weight for height or wasting .

In community based studies ,on the other hand ,MUAC appears superior predicator of childhood morality compared with height and weight based anthropometric indicators .This had led to the proposal of MUAC as an additional screening tool in anon emergency situation

(54).Just the use of a fixed cut off point may result in wasting being over diagnosed among older ones .

The MUAC is measured with a non-stretch tape or with a strip of x-ray film coloured to show cut-off limits (Shakir s strip)

1-Reading >13.5 cm, the green colour zone of the adequately nourished children .

2-Between 13.5_12.5, the yellow colour zone of moderately nourished children .

3-Below 12.5 cm ,the red colour zone that indicates severe malnutrition .(3)

Severe Protein Energy Malnutrition:

Clinical manifestation:

Kwashiorkor and marasmus are 2 forms of PEM that have been described. The distinction between the 2 forms of PEM is based on the presence (kwashiorkor) or absence (marasmus) of edema and there was syndrome between 2 forms (marasmus kwashiorkor) [1].

Marasmus results of inadequate intake of protein and calories, whereas a child with kwashiorkor has fair-to-normal calorie intake with inadequate protein intake. significant clinical differences between kwashiorkor and marasmus exist [1].

Marasmus: (Infantile atrophy, inanition, athreysia) :- The clinical picture originates from an inadequate calorie intake due to insufficient diet. Some studies suggest that marasmus represents an adaptation to starvation [49,1,2].

Clinical manifestations:

Initially there is failure to gain weight, followed by loss of weight until emaciation results, with loss of turgor of skin that becomes wrinkled and loose as subcutaneous fat disappears. Because fat is lost last form the sucking pads of the cheeks, the infant's face may retain a relatively normal appearance for sometimes before becoming shrunken and wizened. The abdomen may be distended or flat, and the intestinal pattern may be readily visible. Atrophy of muscles occurs, with resultant hypotonia, the temperature is usually subnormal [33]. The rapid response of the marasmic child to high energy diet with weight and height gains and increased body temperature indicates very adequate endocrine reserve [2,47,48]. The pulse may be slow, and the basal metabolic rate tends to be reduced. At first, the infant may be fretful but later becomes irritable. The infant is usually constipated, but the so-called starvation type of diarrhea may appear, with frequent small stools containing mucus [49].

There is no oedema and may be no change in hair colour. They are usually hungry, but dose not tolerate large amount of food and vomit easily [2,3,47,50].

Kwashiorkor:

It's a clinical syndrome which result from a severe deficiency of protein and inadequate caloric intake. Either from lack of intake or from excessive losses of calories due to increase in the metabolic rate caused by chronic infection. Secondary vitamin and mineral deficiencies may contribute to signs and symptoms. Kwashiorkor means Diposed child, the condition may became evident from early infancy to about 5 yr of age, usually after weaning from the breast. Although gains in height and weight are accelerated with treatment, these measurements never get equal to those of consistently well-nourished children [49].

Clinical manifestation:

Early clinical evidence include lethargy and apathy, when well advanced, it results in inadequate growth, lack of satmine, loss of muscular tissue, increased susceptibility to infections, and edema. Secondary immunodeficiency is one of the most serious and constant features [37,49-52]. The child may develop anorexia, flabbiness of subcutaneous tissues, and loss of muscle tone. The liver may enlarge early or late; fatty infiltration is common, and hepatic export proteins are reduced. Edema usually develops early; failure to gain weight may be masked by edema, which is often present in internal organs before it can be recognized in the face and limbs. Renal plasma flow; glomerular filtration rate, and renal tubular function are decreased. The heart may be small in the early stages of the disease but is usually enlarged later.

Dermatitis is common, darkening of the skin appear in irritated areas but not in areas exposed to sunlight-a contrast to the situation in pellagra. Dyspigmentation may occur in these areas after desquamation, or it may generalized. The hair is often sparse and thin and loses its elasticity. In dark hair children, dyspigmentation may result in streaking red or grey hair colour (hypochromotrichia). A further more serious manifestation is that of weeping dermatosis resembling burns. In some children petachia may be present. Cheilosis and angular stomatitis are common [2,3,49].

Marasmic kwashiorkor:

This is a syndrome which has the characteristics of both kwashiorkor and marasmus. These children presents with gross failure to thrive and their weight for age is less than 60%. In addition they have lower limbs oedema [2,13].

Pathophysiology:

Malnutrition affects virtually every organ system. Dietary protein is needed to provide amino acids for synthesis of body proteins and other compounds that have a variety of functional roles. Energy is essential for all biochemical and physiologic functions in the body. Furthermore, micronutrients are essential in many metabolic functions in the body as components and co-factors in enzymatic process[1].

Pathophysiological changes associated with PEM can be describe as (53)

(1) Body composition changes

(2) Metabolic changes

(3) Anatomic changes

Body composition

Body mass: Body mass is significantly decreased in a heterogeneous way(53).

Fat mass: Fat stores can decrease to as low as 5% of the total body weight and be macroscopically undetectable. The remaining fat is usually stored in the liver as is often observed in kwashiorkor but also to a lesser extent in marasmus.

***Total body water**:* The proportion of water content in the body increases with the increased seriousness of PEM and is associated with loss of fat mass, which is poor in water. The proportion of extra cellular water also is present, in marasmus or in mixed forms of PEM. The increase in extra cellular water is proportional to the increase in the total body water.

Protein mass: Mainly represented by muscle and some organs (e.g. heart), protein mass can decrease up to 30% in the most serious forms. The muscle fibers are thin with loss of saturation. Muscle cells are atrophic, and muscle tissue is infiltrated with fat and fibrous tissue. Total recovery is long but it seems possible [56].

Other organ mass like the brain, skeleton and kidney are preserved, whereas the liver, heart, pancreas, and digestive tract are the first to be affected [53,54].

Minerals and vitamins:

Potassium: Potassium is the electrolyte most studied in marasmus. Total body potassium deficit is associated with decreased muscle mass, poor intake and digestive losses. This potassium deficit, which can reach 15 mEq/kg, contributes to hypotonia, apathy and impaired cardiac function [1,55,56,57].

Other electrolytes, plasma sodium concentration is generally within the reference range but it can be low, which is then considered asign of a poor prognosis. However, intracellular sodium level is elevated in the brain, muscle and red and white blood cells, explaining the sodium excretion in the first days of recovery [53].

Other minerals:- deficiency of calcium, phosphorus and magnesium in the stores also exist. Iron deficiency anemia is consistently observed in PEM. However, in the most serious forms, iron accumulates in the liver, most likely because of a deficit in the transport protein. These patients are at higher risk of mortality. Therefore, iron is supplemented only after the acute recovery phase is completed [56]. Zinc, selenium, and magnesium are more significantly deficient in marasmus [8.1,54]. Several studies have shown improved recovery from malnutrition and decreased mortality with supplementation of these 3 micronutrients [1,54,58,59].

Vitamins: Both fat-soluble and water-soluble vitamins must be systematically administered. Vitamin A is essential to retinal function, has atrophic effect on epithelial tissues, and plays a major roles as an antioxidant agent vitamin A deficiency affects visual, digestive, respiratory and urinary functions. Furthermore, vitamin A supplementation programs have resulted in decreased mortality and morbidity, in particular, during diarrhoeal disease and measles [53].

Metabolic Changes:

Energy metabolism:

With reduced energy intake, a decrease in physical activity occurs along with a slower and, ultimately, lack of growth-weight loss occurs first by a decrease in fat mass, then a decrease in muscle mass, which is clinically measured by changes in arm circumference. Muscle mass loss result in a decrease of energy expenditure. Reduced energy metabolism can impair the response of patients with PEM to change in environmental temperature, resulting in an increased risk of hypothermia. Furthermore, during infection, fever is reduced compared to a well-nourished patient [(1)].

Protein metabolism: Intestinal absorption of amino acids is maintained, despite the atrophy of the intestinal mucosa. Protein turnover is decreased (up to 40% in severe forms) and protein-sparing mechanisms regulated by complex hormonal controls which redirect amino acids to vital organs. Amino acids liberated from the loss of muscle mass are recycled in priority by the liver for the synthesis of essential proteins [(56)].

Albumin: An albumin concentration lower than 30 g/l is often considered as the threshold below which edema develops. However in marasmus, albumin concentration can occasionally be below this value without edema[56].

Carbohydrate metabolism:

Glucose level is often low initially, and glycogen stores are depleted. Also, a certain degree of glucose intolerance of unclear etiology may exist, possibly associated with a peripheral resistance to insulin or with hypokalemia [1,54].

Fat metabolism:

Dietary fat are often malabsorbed in the initial phase of marasmus malnutrition. The mobilization of fat stores for energy metabolism takes place under hormonal control by adrenaline and growth hormone. Blood lipid levels are usually low and serious deregulation of lipid metabolism can occur. Mainly during kwashiorkor and rarely during marasmus [53] .

Anatomic Changes:

Digestive tract:

The digestive tract, from the mouth to the rectum, is affected. The mucosal surface is smooth and thin, and secretory functions are impaired. The decrease in gastric hydrochloric acid (HCL) excretion results in bacterial overgrowth in the duodenum. The peristalsis is slow.

In addition to the anatomic changes associated with PEM, the frequent intestinal infection by viruses, bacteria, and toxins also contribute to the changes in digestive tract [53,54].

Liver volume decreased mainly in marasmus and enlarged mostly in kwashiorkor. Liver synthetic function is usually preserved, although protein synthesis is decreased, as reflected by the decreased albumin and prealbumins levels. The neoglycogenesis is decreased. Further increasing the risk for hypoglycemia [53,54].

Endocrine system:

The main perturbations are observed in the thyroid, insulin, and growth hormone system. As in any stressed state, the adrenergic response is activated. This response is functional in marasmus but less so in kwashiorkor. Furthermore, in serious marasmus, a significant degree of hypothyroidism, with a decreased in the size of the thyroid gland and repercussions on the brain function and psychomotor development exists. In less severe forms, the impaired thyroid function has fewer clinical consequences. Insulin level are low lead to glucose intolerance, specially during kwashiorkor growth hormone levels are initially within the reference range, but progressively decrease with time[1].

Hematopoietic system:

A moderate normochromic or slightly hypochromic anemia is usually present with normal red blood cell size. Iron and folate deficiencies, intestinal parasites, malaria, and other chronic infection exacerbate the anemia [53].

Immune system:

All aspect of immunity are diminished, lymph glands, tonsils and the thymus are atrophied and cell mediated (T-cell) immunity is severely depressed.

Further more, IgA levels in secretions are reduced and compliment components are low and phagocytes do not kill ingested bacteria efficiently resulting in tissue damage. Also inflammatory responses of white cells to the affected area and acute phase immune response is diminished(1).

Typical signs of infection, such as an increases white cell count and fever, are frequently absent [54].

Brain and Nervous System:

Early studies of malnourished children showed changes in the developing brain, including, a slowed rate of growth of the brain, lower brain weight, thinner cerebral cortex, decreased number of neurons, insufficient myclinization, and changes in the dendritic spines. More recently, neuroimaging studies have shown severe alteration in the dentritic spine apparatus of cortical neurons in infants with sever protein calorie malnutrition(53,54).

Cardiovascular system:

Cardiac muscle fiber is thin, and contractility of the myofibrils is impaired. Cardiac output, is decreased in the same proportion as the weight loss(1). Bradycardia and hypotension commonly occur in severe forms of malnutrition. Electrolyte imbalances present during marasmus modify the electrocardiography ECG findings. With this impaired cardiac function, any increase of intravascular volume during rehydration or blood transfusion can result in a significant cardiac insufficiency. With the rapid metabolic, energy and electrolyte changes of the initially phase of renutrition, there is a period of high risk for arrhythmia or cardiac arrest. Therefore, close clinical monitoring is critical in children with circulatory compromise(53).

Deficiency of Fat Soluble Vitamins:

Children with protein-energy malnutrition also may have deficiencies of the fat soluble vitamin A, D, E and K.

Vitamin A: Vitamin A deficiency is common in the developing world[58]. It is associated with group of ocular signs known as xerophthalmia. The earliest symptom is night blindness, which is followed by xerosis of conjunctiva and cornea[58,59] progression of disease include keratomalasia, ulceration, perforation and scarring of the cornea, prolepses of the lens, and blindness, other features of vitamin A deficiency include follicular hyperkeratosis, purities, growth retardation, and increased susceptibility to infection[60,61].

Vitamin D:

Deficiency of vitamin D, typically caused by dietary deficiency and inadequate exposure to sun light, is associated with hypocalcaemia, hypophosphatemia, and rickets in children [62,63].

Echocardiographic studies revealed left ventricular dysfunction in pretreatment stage of rickets. The most striking echocardiographic finding is the increase in the ratio of interventricular septal thickness to left ventricular posterior wall thickness, these abnormalities were not, however sufficiently severe to be associated with clinical signs of cardiac failure. Cardiomyopathy may develop in rickets This returns to normal after adequate treatment of the rickets [64].

Vitamin E:

Tocopherol deficiency can be associated with a progressive a hemolytic anaemia [64].

Vitamin K:

Deficiency of vitamin K results in a bleeding diathesis. Bleeding may be seen in the skin, gastrointestinal tract-genitourinary, gingiva, lungs, joints, or the central nervous system.

Deficiency of water soluble vitamins:

Deficiency of water-soluble vitamins are seen with protein-energy malnutrition but are less common than are deficiencies of fat soluble vitamins.

Thiamine:

Thiamine (B_1) deficiency is classically associated with beriberi, which is characterized by high output cardiomyopathy and polyneuritis. Infantile beriberi occurs in infant between one and four months of age who have protein-energy malnutrition, the usual causes are receiving unsupplemented hyperalimentation fluid or boiled milk. Also it occurs in infants whose mothers are deficient in thiamine [(66)]. Infant with beriberi have characteristic hoarseness or aphonic cry caused by laryngeal paralysis.

Riboflavin:

Riboflavin (vitamin B_2) deficiency is characterized classically by angular stomatitis, glossitis (magenta tongue) seborrhoeic dermatitis around the nose and scrotum, and vascularization of the cornea [(67)].

Niacin:

Niacin (vitamin B_3) deficiency results in pellagra with dermatitis, diarrhea, dementia, and weakness. The dermatitis is localized to sun-exposed areas of the body. The skin is dry, cracked and hyperpigmented. Watery diarrhea may be pronounced also neurological findings including peripheral neuropathy, loss of memory, emotional instability, toxic psychosis associated with delirium and catatonia, seizures and coma may occur. Oral manifestations include cheilosis, angular fissures, and painful inflammation of the mouth, which may lead to refusal of food [(68)].

Pyridoxine: Pyridoxine (vitamin B_6) deficiency manifests as nonspecific stomatitis, glossitis, cheilosis, irritability, confusion, weight loss, and depression. Peripheral neuropathy occurs in adolescents, where as younger children may develop an encephalopathy with seizures [(66)].

Vitamin B_{12}:

Vitamin B_{12} deficiency is uncommon in children but can occur in exclusively breast-fed infants of vegetarian mothers- deficiency may cause megaloblastic anaemia, neuropathy, and demyelination .

Ascorbic acid

Ascorbic acid (vitamin C) deficiency results in the clinical manifestations of scurvy-Overt clinical scurvy may presents with hemorrhage (petechia, ecchymoses, bleeding gums), follicular hyperkeratosis, hemolytic anaemia and hypochondrosis. Failure to thrive, fragmented hair with a characteristic cork screw appearance are specific features of vitamin C deficiency(68).

Minerals and Trace Elements Deficiencies:

Children with PEM also may be deficient in minerals of trace elements.

Calcium: Phosphate and magnesium-calcium deficiency occurs in conjunction with vitamin D or parathyroid hormone affection .Clinical manifestations of hypocalcaemia include tetany and seizures, severe hypophophatema, pain, and osteomalacia or rickets hypomagnesaemia is typically associated with hypocalcaemia and hypokalaemia and manifests with muscle fasculations tremors or spasm, personality changes and seizure(68).

Iron:

Iron deficiency anaemia is the most common nutritional deficiency in children. Usually it is a mild to moderate microcytic hypochromic anaemia in an otherwise asymptomatic infant or child. Severe iron deficiency anaemia present with lethargy, pallor, irritability, cardiomegally, poor feeding. Tachypnea, and impaired psychomotor and mental development[69,70].

Zinc:

Zinc deficiency was originally described in a group of children with low levels of zinc in their hair, poor appetite. Diminished taste acuity, hypogonadism, and short stature. Now, it is recognized to be associated also with numerous other findings, including alopecia, dermatitis, growth failure, and increased susceptibility to infection[71-73].

Copper:

Copper deficiency was first reported in infants recovering from PEM whose treatment was based on cow's milk. Copper deficiency is associated with a sideroblastic anaemia, neutropenia, failure to thrive, and skeletal abnormalities including osteoporosis, enlargement of costochondral cartilage, cupping and flaring of long bone metaphyses, and spontaneous fractures of the ribs[74.

Selenium:

Selenium deficiency can cause dilated cardiomyopathy with myocardial necrosis and fibrosis. This condition, known as Keshan disease, occurs primarily in children living in rural China[19]. Sporadic cases have been reported in individuals with poor nutritional intake, mostly in individuals on long-term home parentral nutrition[75;76].

Muscle pain, myopathy, loss of hair pigment, and nail bed changes may also occur[75,76].

Iodine:

Moderate iodine deficiency can lead to hyperplasia and hypertrophy of thyroid gland or goiter to maintain an euthyroid state[77]. Severe dietary iodine deficiency results in hypothyroidism. Hypothyroidism during critical early periods of development can lead to permanent mental retardation, hearing impairment, spastic diplegia and strabismus.

Vitamins ,minerals and trace element deficiencies affect the heart through various mechanism . Electrolytes disturbance may cause arrhythmias and electrocardiographic changes. Among vitamin deficiency disease ,beriberi causes the most conspicuous cardiac damage .in patient with malnutrition such as kwashiorkor, the deficiencies are often multiple, and it may be difficult to separate the cardiac lesion of one nutritional disease from that of another .Selenium deficiency is other cause of dilated cardiomyopathy (74) . Severe anemia is common presentation in malnutrition as result of vitamins and iron deficiency, which may be associated with cardiac involvement .Although the cardiac output increases when the hemoglobin is less than 7g/dl significant cardiac enlargement occurs with an extreme reduction in hemoglobin (3_4g or less).The heart rate is rapid, the pulse pressure increased, a systolic flow murmur at the apex or along the left sternal border is usual, diastolic murmurs may occur in the same areas and gallop rhythm is also common (74).

Treatment of severe malnutrition:

Children with severe malnutrition are in danger of death from hypoglycaemia, hypothermia, fluid overload, and undetected infections. However, the child with severe malnutrition must be treated differently because his physiology is abnormal due to reductive adaptation [(54)].

The systems of the body begin to (shut down) with severe malnutrition, the systems slow down and do less in order to allow survival on limited calories. This slowing down in known as reductive adaptation. As the child is treated, the bodys system must gradually "learn" to function fully again. Rapid changes (such as rapid feeding or fluids) would overwhelm the systems, so feeding must be slowly and cautiously increased [54].

The WHO manual management of sever malnutrition guidelines have been developed to improve inpatient treatment of sever malnutrition.

The guidelines are divided in five sections [60]:

A. General principles for routine care (the 10 steps)

B. Emergency treatment of shock and severe anaemia.

C. Treatment of associated conditions.

D. Failure to respond to treatment.

E. Discharge before recovery is complete.

General principles for routine care:

(The 10 steps) [78].

There are ten essential steps:

1- Treat/prevent hypoglycaemia

2- Treat/prevent hypothermia

3- Treat/prevent dehydration

4- Correct electrolyte imbalance

5- Treat/prevent infection

6- Correct micronutrient deficiencies

7- Start cautious feeding

8- Achieve catch-up growth

9- Provide sensory stimulation and emotional support

10- Prepare for follow-up after recovery.

Step 1: Treat/prevent hypoglycemia:

Hypoglycemia and hypothermia usually occur together and are signs of infection check for together and are signs of infection check for hypoglycemia whenever hypothermia is found. Frequent feeding is important in preventing both conditions.

Treatment:

If the child is conscious and dextro stix shows < 3 mmol/l or 54 mg/dl give 50 ml bolus of 10% glucose or 10% sucrose solution orally or by nasogastric (NG) tube. Then feed starter F-75 ever 30 minutes for two hours. Then give antibiotics and two hourly feeds, day and night.

If the child is unconscious, lethargic or convulsing give IV sterile 10% glucose (5 ml/kg) followed by 50 ml of 10% glucose or sucrose by NG tube then starter F-75 as above, always follow up the blood glucose level, rectal temperature and level of consciousness. Prevention of hypoglycemia by feeding two-hourly and always by giving feeds throughout the night [79].

Step 2: Treat/prevent hypothermia:

If the rectal temperature is < 35.5^{o}C (< 95.9^{o}F) feed immediately and rewarm the child either covering with a warmed blanket and placing a heater or lamp nearby, or by putting the child on the mother's bare chest (skin to skin), and covering them and give antibiotics . follow by body temperature, feel for warmth and do serial blood glucose level. To prevent hypothermia , the baby should feed throughout the day and night , and should be kept covered and away from draughts and to keep him dry . Also avoid exposure and let child sleep with mother. If child's temperature is too low to register on an ordinary thermometer, assume the child has hypothermia.

Step 3: Treat/prevent dehydration:

Low blood volume can co-exist with oedema and the use of IV route for rehydration except in cases and shock is not advise. The standard oral rehydration salts solution (90 mmol sodium/1) contains too much sodium and too little potassium for severely malnourished children. Instead give special rehydration solution for malnutrition. It's difficult to estimate dehydration status in a severely malnourished child using clinical signs alone. So assume all children with watery diarrhea may have dehydration and give ReSoMal 5 ml/kg every 30 min for two hours, orally or by nasogastric tube .Then give 5-10 ml/kg/hr for next 4-10 hours . The exact amount to be given should be determined by how much the child wants, and the on going losses . Replace the Resomal doses at 4, 6, 8 and 10 hours with F-75 if dehydration is continuing at these times, then continue feeding started F-75. During treatment, rapid respiration and pulse rates should slow down and the child should begin to pass urine. Monitor progress of rehydration, observe half-hourly for two hours, then hourly for the next 6-12 hours, recording

- Pulse rate
- Respiratory rate
- Urine frequency

- Stool/vomit frequency

Continuing rapid breathing and pulse during rehydration suggest co-existing infection or overhydration. Signs of excess fluid (overhydration) are increasing respiratory rate and pulse rate, increasing oedema and puffy eyelids. If these signs occur, stop fluids immediately and reassess after one hour.

To prevent dehydration when a child has continuing watery diarrhea, keep feeding with starter F-75 and replace approximate volume of stool losses with Resomal. As a guide give 50-100 ml after each watery stool and encourage breast-feeding.

Step 4: Correct electrolyte imbalance:

All severely malnourished children have excess body sodium even though plasma sodium may be low. Deficiencies of potassium and magnesium are also present and may take at least two weeks to correct. Oedema is partly due to these imbalances, so give:-

- Extra potassium 3-4 mmol/kg/d
- Extra magnesium 0.4 – 0.6 mmol/kg/d
- During rehydration give low sodium rehydration fluid
- Prepare food without salt.

Step 5: Treat/prevent infection:

In severe malnutrition the usual signs of infection, such as fever, are often absent and infections are often hidden, therefore give , routinely on admission , broad-spectrum antibiotics.

Step 6: Correct micronutrient deficiencies:

All severely malnourished children have vitamin and mineral deficiencies. Although anaemia is common, do not give iron initially , but wait until the child has a good appetite and starts gaining weight.

Give vitamin A orally in day1-2-7 of treatment (for children whose age > 12 months give 200,000 IU; for those between age 6-12 months give 100,000 IU; and those less than 0-5 months give 50,000 IU.

Give also the following on daily basis for at least 2 weeks:

- Multivitamin supplement
- Folic acid 1 mg/d (give 5 mg on day I)
- Zinc 2 mg/kg/d
- Copper 0.3 mg/kg/d
- Iron 3 mg/kg/d(but only when gaining weight).

Step 7: Start continuous feeding:

In the stabilization phase, a cautious approach is required because of the child's fragile physiological state and reduced homeostatic capacity. Feeding should be started as soon as possible after admission and should be designed to provide just sufficient energy and protein to maintain the basic physiological processes. Milk-based formulas such as starter F-75 will be satisfactory for most children.

During the stabilization phase, diarrheoa should gradually diminish and oedematous children should lose weight.

Step 8: Active catch-up growth:

In the rehabilitation phase a vigorous approach to feeding is required to achieve very high intakes and rapid weight gain of > 10 g /kg/d. The recommended milk-based F-100 contains 100 kcal and 2.9 g protein/100 ml. modified porridges or modified family foods can be used, provided they have comparable energy and protein concentrations.

Readiness to enter the rehabilitation phase is signaled by a return of appetite, usually about one week after admission. A gradual transition is recommended to avoid the risk of heart failure which can occur if children suddenly consume huge amounts.

Step 9: Provide sensory stimulation and emotional support:

In severe malnutrition there is delayed mental and behavioral development.

Provide:

- Tender loving care
- A cheerful, stimulating environment
- Structured play therapy 15-30 minutes every day .
- Physical activity as soon as the child is well enough
- Maternal involvement when possible (e.g. comforting, feeding, bathing, playing).

Step 10: Prepare for follow up after recovery:

A child who is 90% weight-for-length (equivalent to-ISD) can be considered to have recovered. The child is still likely to have a low weight-for-age because of stunting. Good feeding practices and sensory stimulation should be continued at home. Show parent or career how to

- Feed frequently with energy and nutrient-dense foods.
- Give structured play therapy.

Advise parent or career to:-

- Bring child back for regular follow-up checks
- Ensure booster immunizations are given
- Ensure vitamin A is given every six months

B- Emergency Treatment of Shock and Sever Anaemia:

1- Shock:-

Shock from dehydration and sepsis are likely to co-exist in severely malnourished children. They are difficult to be differentiated with clinical signs only. Children with dehydration will respond to IV fluids. Those with septic shock and no dehydration will not respond. The amount of fluid given is determined by the child's response. Overhydration must be avoided . To start treatment:

- Given oxygen
- Give sterile 10% glucose (5 ml/kg) by IV route
- Give IV fluids (15 ml/kg) over 1 hour. Use Ringer's lactate with 5% dextrose; or half normal saline with 5% dextrose or half-strength Darrow's solution with 5% dextrose.
- Measure and record pulse and respiratory rates every 10 minutes.

- Give antibiotics.

If there are signs of improvement:

- Repeat IV fluids(15 ml/kg) over 1 hour; then
- Switch to oral or NG rehydration with Resomal, (10 ml/kg/h) for up to 10 hours. Give ResoMal in alternate hours with starter F-75 then
- Continue feeding with starter F-75

If the child fails to improve after the first hour of treatment (assume that the child has septic shock. In this case:

- Give maintenance IV fluid (4 ml/kg/h) while waiting for blood.
- When blood is available transfuse fresh whole blood at (10 ml/kg) slowly over 3 hours; then
- Begin feeding with starter F-75

2- Severe anaemia in malnourished children

A blood transfusion is required if

- Hb is less than 4 g./dl
- Or if there is respiratory distress and Hb is between 4 and 6 g/dl.

Give:

- Whole blood 10 ml/kg slowly over 3 hours
- Furosemide 1 mg/kg at the beginning of the transfusion.

If the severely anemic has signs of cardiac failure, transfuse packed cell (5-7 ml/kg) rather than whole blood. Following the transfusion, if the Hb remains less than 4 g/dl or between 4 and 6 g/dl in a child with continuing respiratory distress do not repeat the transfusion within 4 days.

In mild to moderate anaemia, oral iron should be given for two months to replenish iron stores but this should not be started until the child has begun to gain weight.

The Effect of Malnutrition on the Heart:

Malnutrition, regardless of its type, has definite effect on cardiac volume, muscle mass, as well as electrical properties of the myocardium. The systolic functions of the heart are affected more than the diastolic functions and this affection becomes manifest only in severe cases and may constitute a bad prognostic parameter thus necessitating more intense management and strict follow-up of such cases [(65)].

Children suffering from sever malnutrition exhibit cardiovascular abnormalities including hypotension, cardiac arrhythmias, cardiomyopathy, cardiac failure, even sudden death . There were various studies done to evaluated cardiac functions and left ventricular mass in malnourished children [1,78,79,80,81]. Ocal found that in children with severe protein energy malnutrition, that the decrease in LV mass was most prominent in the patients with kwashiorkor. However, cardiac output measured by echocardiography showed no statistically significant difference among all patients with PEM. Fractional shortening FS and ejection fractional (EF), which are the most widely used parameters in the evaluation of left ventricular systolic functions, showed no change in the (PEM) group compared to the control group. Heart rate was not significantly different in the patients with PEM and from the control group (78).

Diastolic function indices such as the early Peak of velocity of mitral inflow (Peak E),the late Peak of A mitral inflow (Peak A);E velocity time integral (E VTI), A velocity time integral (A VTI), E VTI/A VTI radio ; the deceleration time of peak E velocity (EDT)and isovolumetric relaxation time, , were not significantly different in the patients and controls. The study concluded that LV mass and cardiac output were reduced in proportion to decrease in body size in patients with PEM and LV systolic and diastolic functions were preserved in atrophic heart.

In Egypt, a study done by EL-Sayed HL revealed that the electrical properties of the myocardium (assessed by ECG) showed significant decrease of R amplitude and corrected QT interval (QTc) in patients compared to controls with significant improvement after nutritional rehabilitation .Echocardiographic changes showed that cardiac mass index was significantly lower in all groups of malnourished cases compared to the controls with significant increase after nutritional rehabilitation. The study showed that the parameters of left ventricular (LV) systolic function which are the ejection fraction, fractional shortening and velocity of circumferential fiber shortening were not significantly reduced in patients compared to the controls. The diastolic function also showed no significant difference in the E wave/A wave (E/A) ratio between patients and controls. However, the systolic time interval showed significantly high LV pre-ejection index in patients in comparison to controls . Edematous and nonedematous cases did not show any significant difference in ECG and echocardiographic data before or after nutritional rehabilitation. The heart of two severely affected patients uniquely, demonstrated marked decrease of LV end diastolic diameter (LEVDd) together with detection of troponin-1 in their sera (79)

A study done in India(80) investigated 25 children aged 1-5 yrs with (PEM) and compared their left ventricular mass and function to those of 26 (age and sex-matched) healthy children. The mean left ventricular mass in the patients was lower than that in the controls. However, left ventricular mass(g/kg body weight) was significantly increased in the patients suggesting relative cardiac "sparing". The systolic function indices like ejection fraction, percentage fractional shortening, and velocity of circumferential fiber shortening were not significantly different between the patients and normal children. The left ventricular end diastolic volume, stroke volume and cardiac output were reduced in proportion to decrease in body size in the patients, so that the cardiac index was not reduced but slightly increased in these patients. There was no significant difference in any of these parameters of left ventricular function or mass in patients with marasmus, as compared to those of patients with marasmus-kwashiorkor. Amongst the 25 patients, however, 5 patients (20%) had an ejection fraction of less than 50% compared to the other 20 patients. These 5 patients had lower left ventricular mass, lower left ventricular mass ((g)/kg body weight)and worse prognosis.

Phornphatkul C and his colleagues [(80)] in Thailand investigated the cardiovascular status of severely malnourished children before, during and after nutritional rehabilitation. In most children with severe malnutrition cardiac mass was decreased on admission to the hospital and recovered subsequent to nutritional therapy. All children had echocardiographic and Doppler measurements indicative of impaired ventricular function which significantly improved during the course of hospitalization, as evidenced in part by the change in fractional shortening, mean velocity of circumferential fiber shortening and systolic time interval and they concluded that children with (PEM) not only have cardiac muscle wasting, but also have inherent ventricular dysfunction as the result of sever malnutrition that responds to nutritional therapy. Particular care with fluid administration is imperative in the first week of therapy, when heart function is the most compromised [81].

On the other hand, Fuenmayor AJ and his colleagues conducted a study to determine electrocardiogram (ECG) QT interval dipersion and its variability in malnourished children in Venezuela. A conventional ECG was performed for computing the heart rate, heart rate variability, corrected QT interval, and QT interval dispersion. In addition, blood samples were obtained to measure hemoglobin, haematocrit, plasma protein and plasma electrolyte concentration. Findings showed that the corrected heart rate, heart rate variability, and QT interval were similar in malnourished and well nourished children [82].

In Spain Jose L and his colleagues compared heart abnormalities in a group of malnourished children with normal control .They found that plasma levels of albumin, potassium and calcium were lower in malnourished children. QTc and QTd were significantly greater in patients with malnutrition than in control. Left ventricular mass index (LVmi) were significantly lower in malnourished children. The body mass index $(Kg/m)^2$ was the most powerful predictor of the variability .They concluded that important electrocardiographic

and echocardiographic abnormalities have been found in malnourished children associated with their nutritional status. Special precautions must be taken about the possibility of arrhythmias and sudden death related with malnutrition [83].

A study done in Nigeria by Olowonyo MT investigated the electrocardiographic changes in kwashiorkor, and revealed that the ECG abnormalities included sinus tachycardia in 91%. Low QRS amplitude in all patients and prolonged QTc intervals in (17%). Other ECG abnormalities noted were short QTc intervals in three patients (7%) prolonged PR intervals in four patients (9%)and right axis deviation in two patients(5%) the mean serum sodium, potassium, calcium, albumin, hematocrit and cardiothoracic ratio were significantly lower in children with kwashiorkor than in the control, the correlation between the QRS amplitude and serum potassium and calcium was poor. Also, there was poor correlation between heart rate and haematocrit and between QTc intervals and serum calcium and potassium. However, the correlation between the QRS amplitude and cardiothoracic ratio was good. These findings suggest that the ECG changes in kwashiorkor are due to myocardial atrophy [70]. Serial ECG studies done by

Stephen ,which were carried out on 32 cases of severe kwashiorkor and two cases of marasmus. Single readings were also carried out on 10 controls. In those cases who had a bad prognosis, particularly those who died, there was a marked shift of the axis of the mean QRS vector of the limb lead to the right. Those who did not deteriorate showed no such shift, and those who deteriorated but eventually recovered, showed a shift to the left in the recovery phase. No such shift was noted in the two cases of marasmus and the author suggested that this shift in mean QRS vector could be a useful and accurate prognostic guide [85].

Justification

(1) Malnutrition is a common paediatric problem in Sudan and the different types of malnutrition was found to affect the heart.

(2) No previous study to determine the magnitude of cardiovascular affection in children with malnutrition, was done in Sudan before .

Objectives

(1) To study the cardiac clinical manifestations, and echocardiographic abnormalities in children with malnutrition.

(2) To compare heart abnormalities in a group of malnourished children with a control group and to describe their predictive values.

Table (1) Echocardiography findings in children with protein energy malnutrition (Marasmus, Marasmus kwashiorkor and kwashiorkor)

Difference between mean of each subclass of PEM and control group were tested by independent *t* test and it is statistically significant if P value (sig) < 0.05)

	Classification of malnutrition (PEM)									Control (n=17)	
	Marasmus (n=22)			Marasmus kwashiorkor (n=21)			Kwashiorkor (n=14)				
	Mean	SD	Sig	Mean	SD	Sig	Mean	SD	Sig	Mean	SD
LVM mass in gram	12.32	7.35	0.003	11.10	8.26	0.002	10.23	7.93	0.004	22.35	12.03
LVM index	36.67	20.12	0.136	33.05	21.03	0.055	23.88	18.56	0.005	47.58	23.45
Left ventricular septal thikness (Systolic)	0.71	0.29	0.789	0.66	0.12	0.072	0.73	0.23	0.958	0.73	0.11
Left ventricular septal thikness (Diastolic)	0.56	0.13	0.291	0.53	0.10	0.109	0.55	0.10	0.210	0.62	0.21
Posterior wall thickness (Systolic)	0.59	0.14	0.184	0.56	0.11	0.039	0.54	0.14	0.045	0.66	0.18
Posterior wall thickness (Diastolic)	0.42	0.09	0.147	0.43	0.10	0.265	0.42	0.10	0.245	0.47	0.12
Left ventricular dimention (Systolic)	1.58	0.26	0.385	1.54	0.26	0.189	1.40	0.27	0.020	1.66	0.29
Left ventricular dimention (Diastolic)	2.36	0.28	0.144	2.28	0.55	0.099	2.32	0.41	0.136	2.61	0.65
Ejection fraction	66.68	8.17	0.002	66.40	9.65	0.005	71.46	10.05	0.333	74.69	6.73
Fractional shorten	35.41	6.51	0.004	35.35	7.09	0.007	39.46	8.84	0.553	41.13	4.98
E wave	0.81	0.29	0.038	0.77	0.13	0.002	0.80	0.18	0.016	1.00	0.25
A wave	0.51	0.24	0.558	0.62	0.41	0.332	0.48	0.20	0.333	0.55	0.21
E\A	1.88	1.18	0.685	1.52	0.52	0.082	2.04	1.11	0.989	2.03	1.13
LVM\Wt (kg)	2.01	1.19	0.564	1.62	1.13	0.657	1.11	0.66	0.051	1.79	1.16

Table (2) Echocardiography findings in children with protein energy malnutrition

Difference between mean of PEM and control group were tested by independent *t* test and it is statistically significant if P value (sig) < 0.05)

	PEM (n=57)			Control (n=17)	
	Mean	SD	Sig	Mean	SD

LVM mass in gram	11.38	7.74	0.002	22.35	12.03
LVM index	32.34	20.38	0.024	47.58	23.45
Left ventricular septal thikness (Systolic)	0.69	0.22	0.414	0.73	0.11
Left ventricular septal thikness (Diastolic)	0.55	0.11	0.165	0.62	0.21
Posterior wall thickness (Systolic)	0.56	0.13	0.046	0.66	0.18
Posterior wall thickness (Diastolic)	0.42	0.09	0.155	0.47	0.12
Left ventricular dimention (Systolic)	1.52	0.27	0.100	1.66	0.29
Left ventricular dimention (Diastolic)	2.32	0.42	0.092	2.61	0.65
Ejection fraction	67.71	9.25	0.002	74.69	6.73
Fractional shorten	36.35	7.39	0.005	41.13	4.98
E wave	0.80	0.21	0.006	1.00	0.25
A wave	1.58	7.89	0.341	0.55	0.21
E\A	1.79	0.99	0.443	2.03	1.13
LVM\Wt (kg)	1.65	1.11	0.675	1.79	1.16

Table (3) Echocardiography findings in children with protein energy malnutrition in relation to age and sex

Difference between mean of each group and control group were tested by independent t test and it is statistically significant if P value (sig) < 0.05)

	Age					**Gender**				
	<=18 months (n=32)		**> 18 months (n=25)**		Sig	**Male (n=22)**		**Female (n=35)**		Sig
	Mean	SD	Mean	**SD**		Mean	SD	Mean	**SD**	
LVM mass in gram	12.20	9.28	16.55	10.60	0.162	13.90	9.24	13.95	10.55	0.508
LVM index	33.05	21.46	40.20	22.34	0.300	37.15	21.93	35.06	22.16	0.340

Left ventricular septal thikness (Systolic)	0.67	0.14	0.74	0.27	0.160	0.68	0.20	0.71	0.20	0.705
Left ventricular septal thikness (Diastolic)	0.55	0.16	0.58	0.12	0.674	0.53	0.09	0.58	0.17	0.203
Posterior wall thickness (Systolic)	0.57	0.15	0.62	0.13	0.444	0.60	0.14	0.58	0.15	0.033
Posterior wall thickness (Diastolic)	0.43	0.10	0.44	0.09	0.700	0.45	0.10	0.43	0.10	0.035
Left ventricular dimention (Systolic)	1.50	0.23	1.63	0.32	0.021	1.54	0.24	1.56	0.30	0.695
Left ventricular dimention (Diastolic)	2.29	0.54	2.54	0.39	0.012	2.41	0.49	2.37	0.51	0.120
Ejection fraction	69.67	9.37	68.72	9.05	0.486	71.44	9.03	67.95	9.12	0.228
Fractional shorten	37.76	7.62	36.93	6.57	0.491	39.30	7.58	36.27	6.74	0.187
E wave	0.81	0.21	0.89	0.28	0.676	0.85	0.25	0.84	0.23	0.726
A wave	0.53	0.21	2.60	11.05	0.326	2.48	10.68	0.52	0.19	0.324
E\A	1.81	0.96	1.92	1.12	0.959	1.84	0.99	1.86	1.05	0.606
LVM\Wt (kg)	1.69	1.14	1.68	1.08	0.711	1.84	1.22	1.58	1.03	0.234

Table (4) Descriptive analysis of numerical variables under study

	N		Mean	Std. Deviation	Minimum	Maximum
	Valid	Missing				
Age in months	57	0	19.23	7.201	8	36
Duration of hospital stay in days	57	0	11.65	9.259	1	49
Family income	53	4	280,962SP	157243.8	50,000	600,000
Weight	57	0	6.4781	1.37964	3	10
Height	57	0	70.4035	10.01447	40	87
Surface area	57	0	0.354798	0.0574234	0.2108	0.4714

Respiratory rate	52	5	31.37	4.257	20	40
Hb level	55	2	8.7255	2.17087	5.2	14.7
PCV	55	2	28.3636	5.50311	18.2	54
Serum albumin	51	6	2.6961	0.7668	1.2	4.9
Serum K	54	3	3.4889	0.68313	2.4	5.6
Serum Ca	52	5	7.6846	0.68123	5.7	9
Serum Na	54	3	133.4259	7.83221	118	150
LVM mass in gram	56	1	11.38	7.736	1	34
LVM index	56	1	32.343	20.37601	2.4	94.4
Left ventricular septal thickness (Systolic)	55	2	0.6938	0.22175	0.42	1.79
Left ventricular septal thickness (Diastolic)	56	1	0.545	0.1117	0.34	0.93
Posterior wall thickness (Systolic)	53	4	0.5643	0.12886	0.23	0.86
Posterior wall thickness (Diastolic)	56	1	0.4243	0.09147	0.29	0.65
Left ventricular dimension (Systolic)	56	1	1.5221	0.26601	0.91	2.4
Left ventricular dimension (Diastolic)	56	1	2.3168	0.42451	0.29	3.17
Ejection fraction	55	2	67.7091	9.25097	43	90
Fractional shorten	55	2	36.3455	7.38672	20	59
E wave	55	2	0.7953	0.21355	0.48	1.83
A wave	55	2	1.5775	7.88868	0.19	59
E\A	55	2	1.794364	0.9866475	0.62	6.5
LVM\Wt (kg)	56	1	1.654327	1.1050674	0.0128	5.23

Table (4) Echocardiography findings in children with protein energy malnutrition in relation to Hb level

Difference between mean of each group were tested by independent t test and it is statistically significant if P value (sig) < 0.05)

	Hb level	Mean	Std. Deviation	Sig (Low*Normal)	Sig (Low*High)	Sig (Normal*High)
LVM mass in gram	Low	11.51	7.759	0.015	0.574	0.045
	Normal	7	2.898			
	High	13.2	5.762			
LVM index	Low	32.9374	21.12085	0.007	0.456	0.023
	Normal	20.6883	6.3561			
	High	38.78	14.76218			
Left ventricular septal thikness (Systolic)	Low	0.6955	0.24405	0.339	0.415	0.154
	Normal	0.625	0.1446			
	High	0.752	0.12112			
Left ventricular septal thikness (Diastolic)	Low	0.5367	0.11476	0.742	0.492	0.644
	Normal	0.55	0.08509			

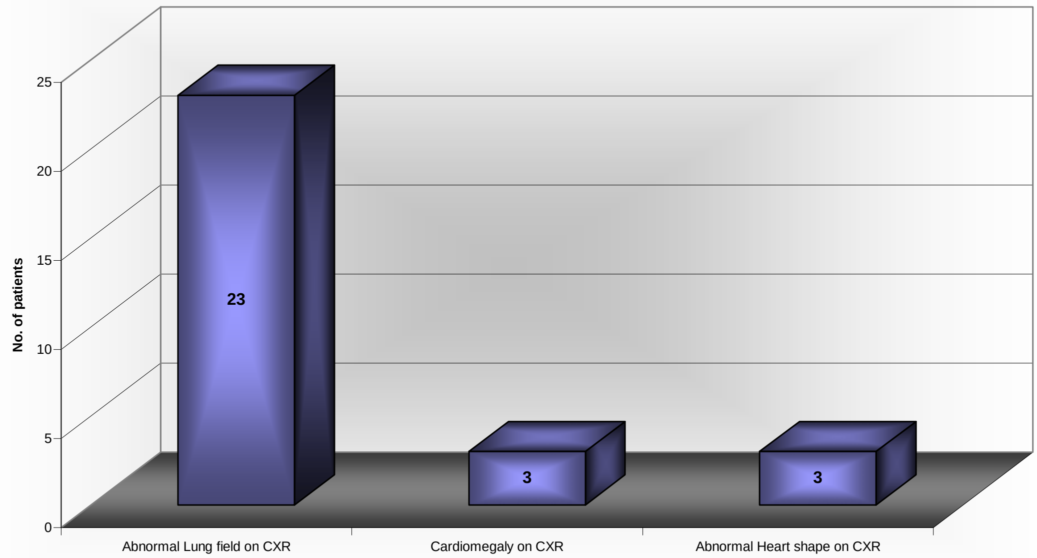
	High	0.584	0.13649			
Posterior wall thickness (Systolic)	Low	0.5678	0.13022	0.38	0.979	0.656
	Normal	0.53	0.08649			
	High	0.57	0.17306			
Posterior wall thickness (Diastolic)	Low	0.4223	0.09167	0.077	0.166	0.031
	Normal	0.3867	0.03204			
	High	0.508	0.11256			
Left ventricular dimension (Systolic)	Low	1.5386	0.27971	0.176	0.355	0.784
	Normal	1.4483	0.11548			
	High	1.412	0.26148			
Left ventricular dimention (Diastolic)	Low	2.3242	0.44659	0.102	0.953	0.339
	Normal	2.1683	0.14825			
	High	2.334	0.32647			
Ejection fraction	Low	67.1395	8.95646	0.453	0.028	0.026
	Normal	63.8	8.67179			
	High	77.8	7.39594			
Fractional shorten	Low	35.8372	6.86235	0.394	0.008	0.036
	Normal	33	6.40312			
	High	45	8.3666			
E wave	Low	0.8137	0.22656	0.102	0.518	0.15
	Normal	0.6657	0.19372			
	High	0.788	0.03834			
A wave	Low	1.9324	9.1375	0.355	0.326	0.497
	Normal	0.5957	0.14246			
	High	0.51	0.23622			
E\A	Low	1.83249	0.959864	0.007	0.762	0.253
	Normal	1.18	0.41227			
	High	2.044	1.431164			
LVM\Wt (kg)	Low	1.73862	1.158794	0.007	0.448	0.035
	Normal	1.08667	0.333806			
	High	2.118	0.959099			

Table (5) Echocardiography findings in children with protein energy malnutrition in relation to Hb level among different age group.

Difference between mean of each group were tested by one way ANOVA test and it is statistically significant if P value (sig) < 0.05)

	Age in months						
	18 months or less				More than 18 months		
	Hb level				Hb level		
	Low	Normal	High	Sig	Low	Normal	Sig
LVM mass in gram	9.77	6.25	13.2	0.328	13.33	8.5	0.408
LVM index	29.9773	21.3825	38.78	0.426	36.0386	19.3	0.276
Left ventricular septal thikness (Systolic)	0.6395	0.625	0.752	0.293	0.7514	0.625	0.575
Left ventricular septal thikness (Diastolic)	0.5032	0.5625	0.584	0.196	0.5719	0.525	0.624
Posterior wall thickness (Systolic)	0.5505	0.54	0.57	0.948	0.585	0.51	0.392
Posterior wall thickness (Diastolic)	0.42	0.3875	0.508	0.122	0.4248	0.385	0.548
Left ventricular dimention (Systolic)	1.4895	1.465	1.412	0.743	1.59	1.415	0.488
Left ventricular dimention (Diastolic)	2.2227	2.09	2.334	0.729	2.4305	2.325	0.688
Ejection fraction	66.8182	58.3333	77.8	0.007	67.4762	72	0.525
Fractional shorten	35.5455	29	45	0.008	36.1429	39	0.588
E wave	0.7959	0.67	0.788	0.622	0.8342	0.66	0.149
A wave	0.5277	0.6325	0.51	0.668	3.5589	0.5467	0.707
E\A	1.688636	1.0875	2.044	0.192	1.998947	1.303333	0.359
LVM\Wt (kg)	1.719545	1.1375	2.118	0.429	1.758567	0.985	0.36

Fig. (21) Distribution of the study cases according to X ray findings (n=57)



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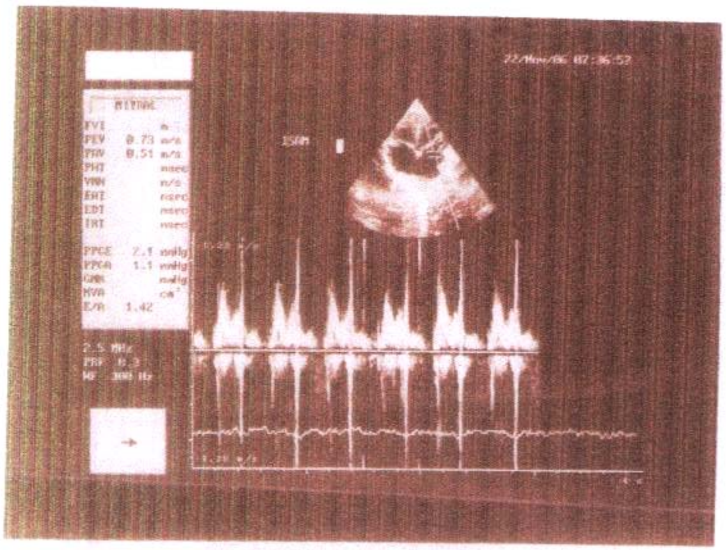
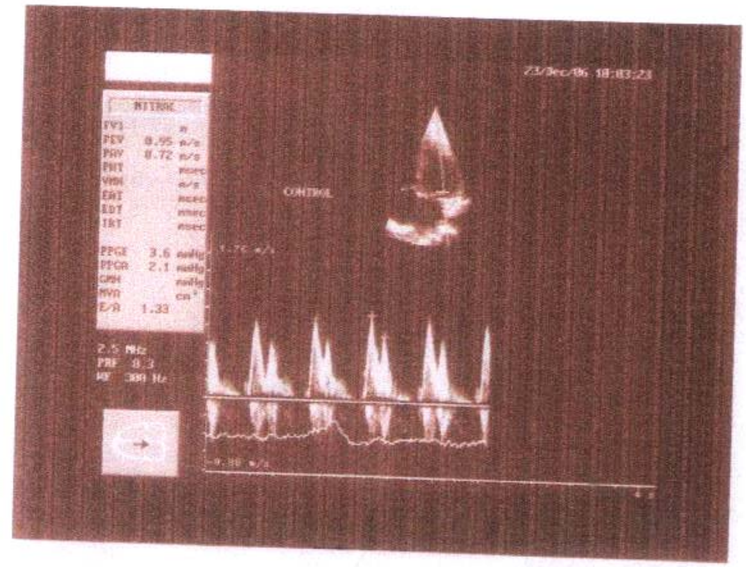
Appendix:

Echocardiographic ,abnormalities in (PEM)



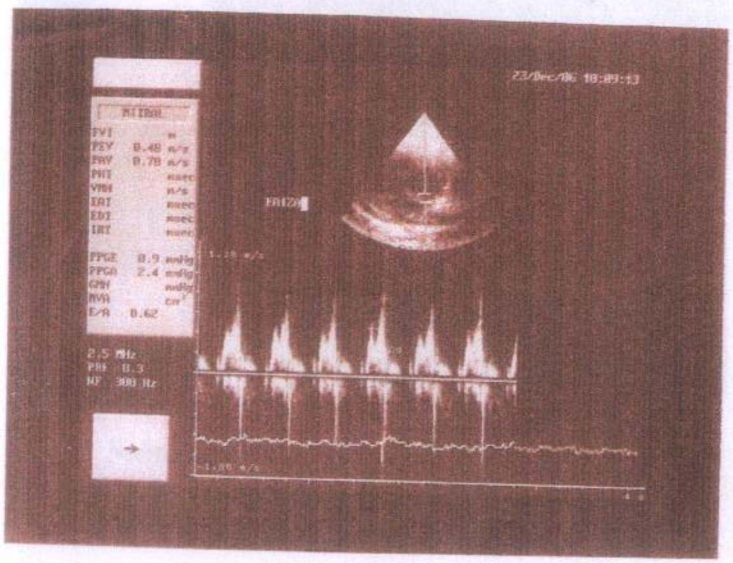
Abnormal A and E waves
in children with (PEM)



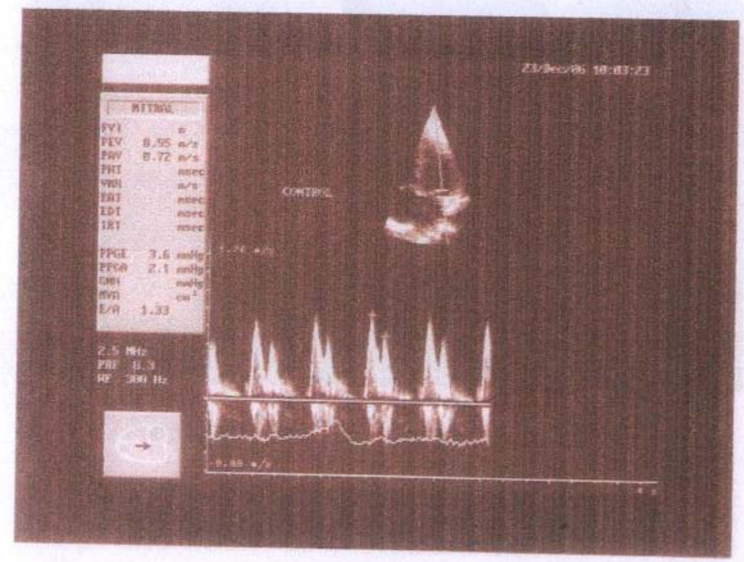
Normal A and E waves in control

Appendix:

Echocardiographic abnormalities in (PEM)



Reverse E and A waves in children with (PEM)



Normal A and E waves in control

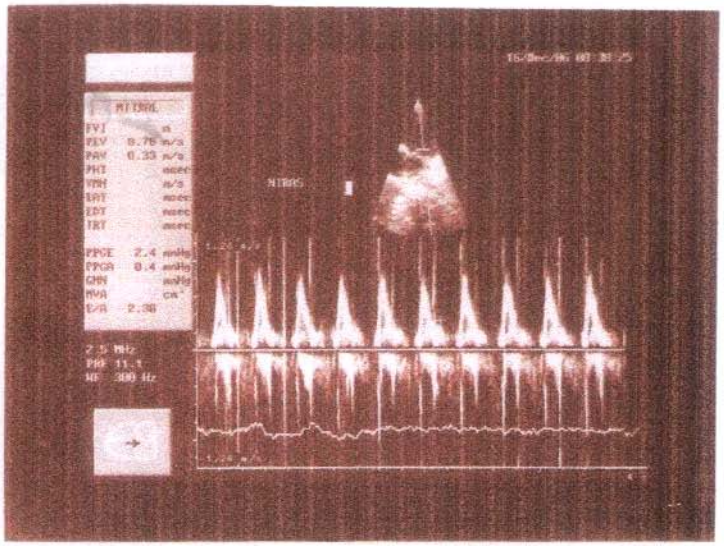
Appendix:

Echocardiographic abnormalities in (PEM)

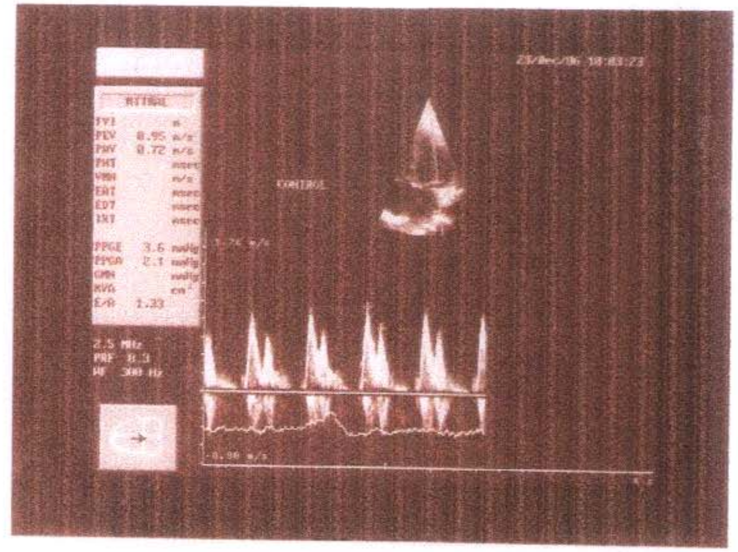
Pericardial effusion in children with PEM

Appendix:

Echocardiographic abnormalities in (PEM)



Summation of A and E waves in children with (PEM)



Normal A and E waves in control

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